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Case Report Open access

Acquired Vitamin K Deficiency Presenting as a Catastrophic GI Bleed in a Hospitalized Patient

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Case Report

Acquired coagulopathy presenting as unexplained bleeding has been described in many critically ill hospitalized patients. The most common causes are DIC (Disseminated intravascular coagulation), renal or hepatic failure, Sepsis induced thrombocytopenia, HIT (Heparin induced thrombocytopenia), malignancy, acquired antibodies to clotting factors, drugs (anticoagulants, antibiotics), severe Vitamin K deficiency. We report a rare case of GI Bleed secondary to acquired Vitamin K deficiency.

Case Description

72 y/o male with history of Insulin dependent Diabetes mellitus, hypertension, hyperlipidemia was brought to the ER from nursing home with frequent symptomatic hypoglycemic episodes. History was positive for chronic poor PO intake, and 2-day history of abdominal discomfort, dysuria and loose stools. He was found to have tenderness in left lower quadrant, guaiac positive stool and occult blood in urine. Initial labs showed Hb=11.7, WBC=5.7, platelet=238, creatinine=1.5, albumin=1.8, pre-albumin=8 (normal 18-45), AST=13, ALT<6, ALP=118, INR=1, PT=11, PTT=37.

Urinalysis showed positive leucocyte esterase and 80 WBCs. CT abdomen showed recto sigmoid colitis. The patient was started on ceftriaxone and metronidazole, made NPO for 2 days, and slowly advanced to a regular diet by day 4. On day 6, he had a massive lower GI Bleed with hemodynamic instability requiring ICU transfer. Technetium scan showed bleeding from recto-sigmoid area.

Stat labs showed INR>10, PT>80, PTT>200, Hb=8.8, platelets=196, AST=28, ALT<6, ALP=127, Creatinine=2.89. Fibrinogen, FDP, DDimer levels were normal. Repeat labs showed same values which ruled out error. PT reported no prior bleeding episodes or family history of bleeding disorders. He was NOT on warfarin at any time and only received Heparin 5000 units BID subcutaneously for VTE prophylaxis during the hospital stay. Individual clotting factors, HIT antibodies were not measured.

PT, PTT corrected in mixing studies. The patient received 5 mg of IV vitamin K, 4 Units of fresh frozen plasma and 2 units of packed red cell transfusion. GI Bleed resolved with reversal of coagulopathy and patient had an uneventful hospital course (Table 1).

LAB Value	Day 1	Day 6	Day 10	Day 12 (at discharge)
Hb	11.7(MCV=95)	11,4	8.8	9.4
Platelet	238	228	196	155
PTT	37		>200	41
PT	11		>80	12
INR	1		>10	1.5
Bun/Creatinine	19/1.5		28/ 2.89	26/2.7
Albumin	1.8	1.4	2.1	2.33
Pre-albumin (normal 18-45)	8			
AST	13	22	28	21
ALT	<6	<6	<6	<6
ALP	118	117	127	117
Total bilirubin	0.1	0.1	0.2	0.3
Total protein	3.3	3.1	3.3	3.3

Table 1: Lab values trend of the patient during hospital course

Discussion

Bleeding secondary to Vitamin K def has classically been associated in infants as Hemorrhagic disease of newborn and administering Vitamin K subcutaneously to all newborns is now a universal practice.

However, acquired vitamin K deficiency in adults manifesting as overt spontaneous bleeding is a rare phenomenon. Vitamin K acts a co-factor in Gama-carboxylation of factors II, VII, IX, X. Vitamin K deficiency results in release of undercarboxylated Vitamin K dependent (VDK) proteins, (known as PVKAs, protein induced vitamin K absence) that have reduced biological activity and lose the ability to participate in normal coagulation cascade [1]. Because factor VII has the shortest half- life, PT becomes prolonged first. Serum concentration of phylloquinone (K1), Vitamin K1 2, 3-Epoxide (K1 O) and PIVKA-II (undercarboxylated factor II) can be measured, but usually the diagnosis is clinical and of exclusion. The specific Vitamin K concentrations were not measured in our patient, due to unavailability of the test in our hospital.

There are two forms of vitamin K- K1 and K2. Vitamin K1 is usually obtained from diet and homologues of vitamin K2 are synthesized by enteric flora [2]. Humans do not maintain large stores of vitamin K and anything that interrupts the supply from diet or gut bacteria can result in a deficiency [3]. Dietary deficiency can be indicated by overall nutritional status of the patient which can be quantified using various Nutrition assessment scales like PNI (Prognostic Nutritional Index), Prognostic Inflammatory and

Nutritional Index (PINI), The Nutritional Risk Screening 2002 (NRS 2002), Mini-Nutritional Assessment–Short Form (MNA-SF), and Malnutrition Universal Screening Tool (MUST). In our patient the diagnosis of under nutrition as a cause of vitamin K deficiency was clinical based on history of chronic poor oral intake, physical exam findings of undernourishment, weight loss, BMI and pre-albumin level [4]. Reported increasing PTs in volunteers who ate a vitamin K deficient diet, but who did not take any antibiotics [5]. Reported that both starvation and ingesting antibiotics that alter gut flora were both necessary to produce coagulopathy of vitamin k deficiency. Apart from their destructive effect on enteric flora, some of the commonly used antibiotics (like Second and third generation Cephalosporins) possess a direct inhibitory effect on the synthesis of VKD clotting factors. Studies using rat liver microsomal preparations show that N-methy-5-thiotetrazoleside chain in these antibiotics can inhibit the biosynthesis of gama carboxy-glutamic acid residues a metabolic block similar to that imposed by the anticoagulant warfarin [6].

Researchers have been trying to identify the risk factors in hospitalized patients for development of vitamin K deficiency. In a study conducted on patients with abdominal sepsis on antibiotics, the patient-related clinical risk factors identified were age>60 years, presence of renal disease, liver disease, malignancy, recent upper GI/lower GI Surgery, PNI>60, use of ASA/NSAIDS, Cimetidine, bowel sounds absent >5 days, platelets<50,000, baseline PT>15 sec [7]. Another study attempted to identify risk factors in critically ill patients with non-consumptive coagulopathy, and found that Apache II score was the only objective variable that was significantly associated with development of ICU-associated coagulopathy [8]. Another small pilot study on cancer pts with bleeding identified that 22% of pts with an advanced cancer have underlying vitamin K deficiency due to anorexia, effect of chemotherapy, antibiotic treatment. Patients in this study who had 1 bleeding episode and who subsequently received prophylactic vitamin K were found to less likely to develop coagulation abnormalities than who did not [9]. In almost all the reported cases of acquired vitamin K deficiency, the postulated mechanism of overt unexpected bleeding has been an acute vitamin K deficiency superimposed on a chronic deficiency state.

Correction of coagulopathy is usually with administration of intravenous Vitamin K. IV administration has rarely been associated adverse reactions resembling anaphylaxis, mostly attributed to rapid infusion rates (>1 mg/min). Prophylaxis is best achieved by giving vitamin K 4 mg two or three times a week either orally or subcutaneously. Oral preparations are erratically absorbed and failure to correct coagulopathy has been demonstrated even in absence of liver disease. Patients with overt bleeding or those who fail to respond to IV Vitamin K preparations must receive fresh frozen plasma to reverse the coagulopathy.

Conclusion

Several observational studies have stressed the importance of early recognition of patients who are at risk of developing acute Vitamin K deficiency superimposed on a chronic deficiency state. Addressing this before clinically significant bleeding arises can decrease morbidity and mortality. There have been no large scale Randomized controlled trials to further validate this point. We stress that physicians should be aware of acquired Vitamin K deficiency in hospitalized patients especially whose nutrition is inadequate and are being treated with antibiotics. Prophylactic Vitamin K supplementation before overt coagulopathy develops would avoid catastrophic bleeding events.

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